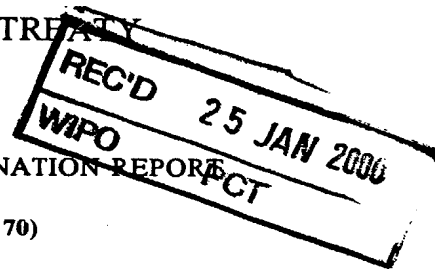


PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference 18547-305-3PC		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US98/05451	International filing date (day/month/year) 19 MARCH 1998	Priority date (day/month/year) 20 MARCH 1997	
International Patent Classification (IPC) or national classification and IPC IPC(7): C12Q 1/68 and US Cl.: 435/6; 436/94			
Applicant AFFYMETRIX, INC.			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 4 sheets.
☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

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Date of submission of the demand 19 OCTOBER 1998	Date of completion of this report 03 JANUARY 2000
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer CARLA MYERS
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

International application No.

I. Basis of the report

☒ the international application as originally filed.

☒ the description, pages 1-15, as originally filed.

pages NONE , filed with the demand.

pages NONE , filed with the letter of _____

pages _____, filed with the letter of _____

☒ the claims, Nos. 1-15, as originally filed.

Nos. NONE, as amended under Article 19.

Nos. NONE , filed with the demand.

Nos. NONE , filed with the letter of _____

Nos. _____, filed with the letter of _____

☒ the drawings, sheets/fig NONE, as originally filed.

sheets/fig NONE , filed with the demand.

_____ sheets/fig NONE , filed with the letter of _____

_____ sheets/fig _____, filed with the letter of _____

2. The amendments have resulted in the cancellation of:

☒ the description, pages NONE

☒ the claims, Nos. NONE

☒ the drawings, sheets/fig NONE

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box Additional observations below (Rule 70.2(c)).

4. Additional observations, if necessary:

NONE

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V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. STATEMENT**

Novelty (N)	Claims <u>1-15</u>	YES
	Claims <u>NONE</u>	NO
Inventive Step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-15</u>	NO
Industrial Applicability (IA)	Claims <u>1-15</u>	YES
	Claims <u>NONE</u>	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-15 lack an inventive step under PCT Article 33(3) as being obvious over Drmanac et al (herein after 'Drmanac'). Drmanac (column 4) discloses methods for determining the sequence of a target nucleic acid by "hybridization of overlapping short oligonucleotide probes of known or predicted sequence to the nucleic acid target serially or simultaneously". It is stated that the probes may comprise all or part of all possible variants of a full or partial sequence. The probes may be composed of oligomers of the same or different sizes and may comprise 6, 7, or 8, etc. nucleotides complementary to a target nucleic acid (columns 3 and 10). The sequencing by hybridization method can be performed under conditions which allow for the discrimination of perfectly matched and mismatched oligonucleotides as short as six nucleotides long (columns 5 and 18). In particular, Drmanac (column 33) teaches methods for sequencing a target nucleic acid by contacting a plurality of oligonucleotide probes with a target nucleic acid under conditions which discriminate between perfectly matched and mismatched oligonucleotide hybrids; detecting positively hybridized oligonucleotides, compiling the sequence of the target nucleic acid from overlapping positively-hybridizing oligonucleotides and repeating the hybridization process with a second set of probes. The compiling step includes linear ordering of subfragments obtained by cyclic detection of overlapped subclones containing subfragments which hybridized with selected probes. Drmanac does not specifically teach determining the "relative hybridization of the probes to the target nucleic acid". However, the step of Drmanac in which perfectly matched hybrids are distinguished from mismatched hybrids is considered to be a step of determining relative hybridization (i.e. presence versus absence of hybridization). The recitation in the instant claims regarding the reference sequence does not further distinguish the claimed invention over that of Drmanac because the array of probes utilized by Drmanac would comprise probes complementary to the reference sequence since the array contains probes comprising all possible sequences. Drmanac further teaches applying the (Continued on Supplemental Sheet.)

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Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):
sequencing method to the analysis of human DNA in order to detect genetic variation and inheritance patterns (column 4).

Claims 1-15 meet the criteria set out under PCT Article 33(4).

NEW CITATIONS

NONE